

10/019264

SPECIFICATION

JC13 Rec'd PCT/PTO 28 DEC 2001

PRODUCTION METHOD OF 1-SUBSTITUTED-1,2,3-TRIAZOLE DERIVATIVES

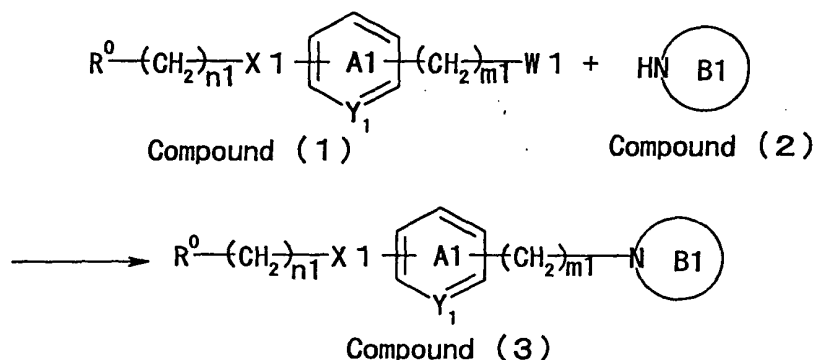
TECHNICAL FIELD

✓ this application is a 371 of PCT/JP01/06145 filed July 16, 2001

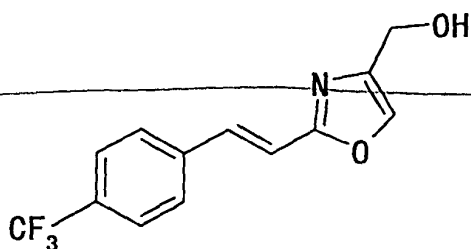
The present invention relates to production methods of
5 intermediates for 1-substituted-1,2,3-triazole compounds having
an inhibitory action on growth factor receptor tyrosine kinases
(especially HER2) useful as pharmaceutical agents.

BACKGROUND ART

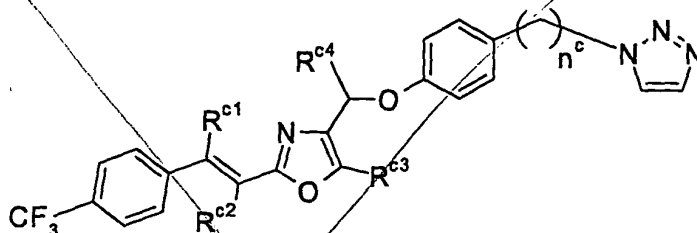
As a production method of an intermediate for a 1-
10 substituted-1,2,3-triazole compound having a tyrosine kinase
inhibitory action, for example, there is mentioned a method
comprising condensing compound (1) of the following formula and
compound (2) of the following formula in the presence of a base
in a solvent inert to the reaction (e.g., aromatic hydrocarbons
15 such as benzene, toluene, xylene etc., ethers such as
tetrahydrofuran, dioxane etc., ketones such as acetone, 2-
butanone etc., halogenated hydrocarbons such as chloroform,
dichloromethane etc., N,N-dimethylformamide, dimethyl sulfoxide,
and a mixed solvent of these) to give the objective compound
20 (3) (JP-A-11-60571, WO 98/03505):



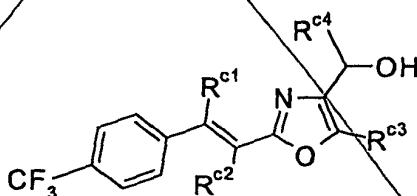
wherein W1 is a leaving group, R⁰ is an optionally substituted
aromatic heterocyclic group, X1 is an oxygen atom, an
optionally oxidized sulfur atom, -C(=O)- or -CH(OH)-, Y₁ is CH
25 or N, m₁ is an integer of 0 to 10, n₁ is an integer of 1 to 5,
the cyclic group



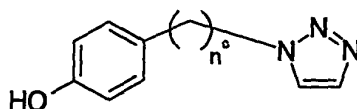
45. A method for producing a compound of the formula



5 wherein n^c is an integer of 1 to 10 and other symbols are as defined in claims 32, or a salt thereof, which comprises subjecting a compound of the formula



10 wherein each symbol is as defined above, or a salt thereof to sulfonylation or halogenation, and reacting the resulting compound with a compound of the formula



wherein n^c is as defined above, or a salt thereof.

(Amended), A crystal of
15 46. 1-[4-[4-[[2-[(E)-2-[4-(trifluoromethyl)phenyl]ethenyl]-1,3-oxazol-4-yl]methoxy]phenyl]butyl]-1H-1,2,3-triazole.

47. The crystal of claim 46, having characteristic peaks at diffraction angles of 6.98, 14.02, 17.56, 21.10 and 24.70